

(b) raising the temperature of the biological sample from a first temperature to a second temperature wherein the second temperature is at least 15°C higher than the first temperature;

(c) holding the biological sample at the second temperature for a predetermined amount of time;

(d) lowering the temperature of the biological sample from the second temperature to at least the first temperature,

(e) holding the biological sample at a temperature at least as low as the first temperature for a pre-determined length of time;

(f) raising the temperature of the biological sample to the second temperature; and

(g) repeating steps c through f, wherein those steps are completed in approximately 10 to 90 [60] seconds [or less].

31. (Amended) The improved method of claim 30 wherein the [capillary vessel defines] sample holding structure has a volume ranging from about [10] 0.1 microliters to about [100] 10,000 microliters.

35. (Amended) An improved method of modifying a biological sample by subjecting the biological sample to multiple cycles of controlled rapid heating and cooling, said method comprising the steps of placing the sample in a [capillary vessel] sample holding structure and thermally cycling the sample by contacting the [capillary vessel] sample holding structure with a heated fluid to raise the temperature of the sample from a first temperature to a second temperature, cooling the sample from said second temperature to a temperature at least as low as the first temperature, and heating the sample back to the second temperature; wherein the difference between the first temperature and the second temperature is at least 15°C, and wherein the heating and cooling step are completed in approximately 10 to 60 seconds, [or less,while] such that the temperature homogeneity in [the] a 10 µL sample during a 30 second cycle is maintained within plus or minus 1°C during the heating and cooling steps.

39. (Amended) The method of claim 37 further comprising the step of cooling

the sample from the denaturation temperature to the annealing temperature at a rate of at least about [1.48°C] 0.5°C per second.

40. (Amended) The method of claim 37 wherein each thermal cycle is completed in [less than] 10 to 60 seconds.

45. (Amended) The method of claim 43 wherein each thermal cycle is completed in [less than] approximately 10 to 60 seconds.

Please add the following new claims:

-- 57. The improved method of Claim 30, wherein the repeating of steps c through f is completed in 30 to 60 seconds.

58. The method of any one of claims 30-35, wherein said sample holding structure is a capillary vessel.--

### REMARKS

Claims 30-45 are pending in the case. The Claims as now pending are provided in the accompanying appendix for the Examiner's convenience.

Claim 30 is amended to state that steps c through f are completed in approximately 10 to 90 seconds. Support is found at page 29, lines 8-12.

Claims 30 and 35 are amended to state that the sample is placed in a sample holding structure. Support is found, for example, at page 32, lines 12-19.

Claim 31 is amended to state that the sample holding structure has a volume ranging from about 0.1 microliters to 10,000 microliters. Support is found at page 33, lines 3-8.

Claims 35, 40 and 45 are amended to state that the heating and cooling steps (35) or the thermal cycle (40, 45), are completed in 10 to 60 seconds. Support is found at page 29, lines 8-12.

Claim 35 is also amended to state that the temperature homogeneity in a 10 µL sample